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NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 12:41:47 ON 18 OCT 2005

=> fil reg

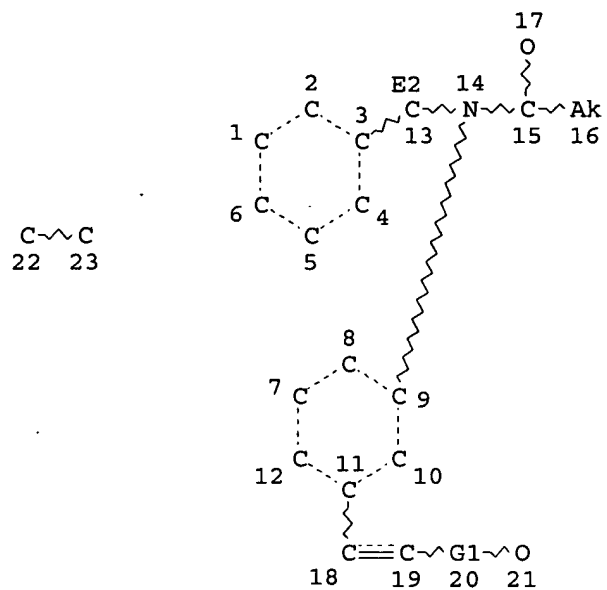
FILE 'REGISTRY' ENTERED AT 12:42:14 ON 18 OCT 2005

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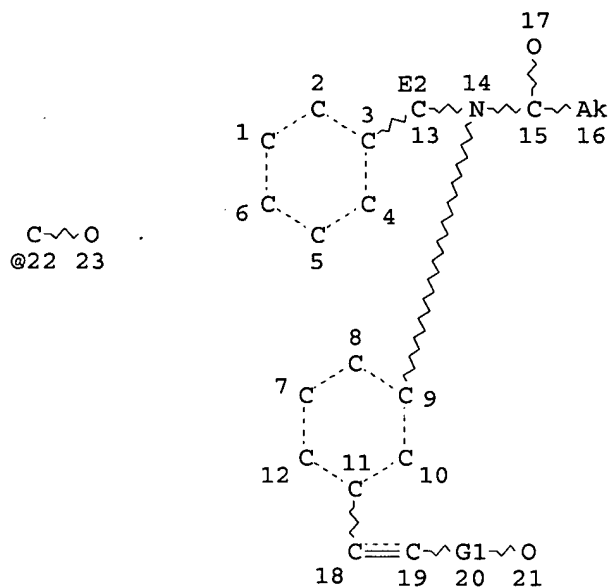
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Property values tagged with IC are from the ZIC/VINITI data file
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:nod 23 o,var g1=ch2/22,dis



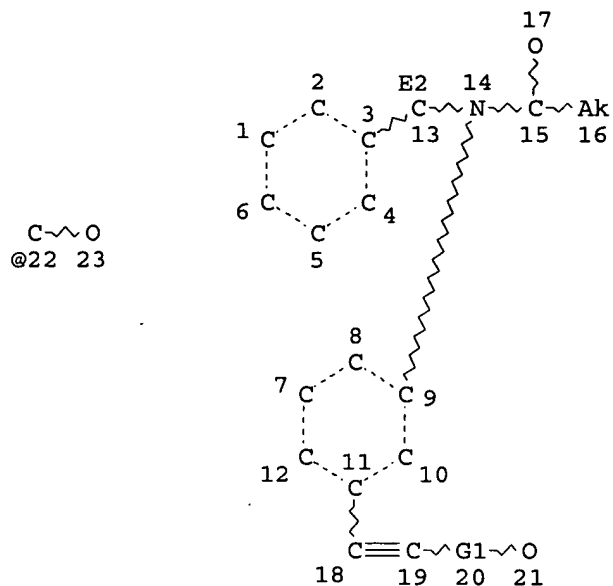
VAR G1=CH2/22

:end

L2 STRUCTURE CREATED

=> str l2

:bon 18-19 t,dis



VAR G1=CH2/22

:end

L3 STRUCTURE CREATED

=> s 12 or 13

SAMPLE SEARCH INITIATED 12:55:05 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 14 TO ITERATE

100.0% PROCESSED 14 ITERATIONS

2 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 56 TO 504

PROJECTED ANSWERS: 2 TO 124

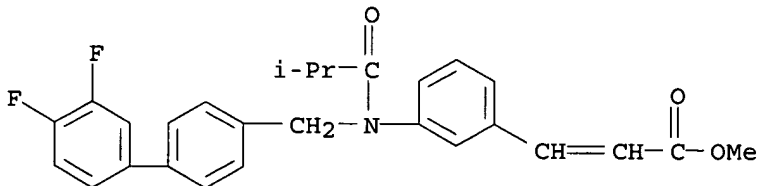
L4 2 SEA SSS SAM L2 OR L3

=> d scan

L4 2 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN

IN 2-Propenoic acid, 3-[3-[[[(3',4'-difluoro[1,1'-biphenyl]-4-yl)methyl](2-methyl-1-oxopropyl)amino]phenyl]-, methyl ester (9CI)

MF C27 H25 F2 N O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d l2 or dl3 ful

L2 HAS NO ANSWERS

'OR DL3 FUL ' IS NOT A VALID STRUCTURE FORMAT KEYWORD

Structure Formats

SIA ----- Structure Image, Attributes, and map table if it contains
data. (Default)

SIM ----- Structure Image.

SAT ----- Structure ATtributes and map table if it contains data.

SCT ----- Structure Connection Table and map table if it contains
data.

SDA ----- All Structure Data (image, attributes, connection table and
map table if it contains data).

NOS ----- NO Structure data.

ENTER STRUCTURE FORMAT (SIA), SCT, SDA, SIM, SAT, NOS:end

=> s l2 or l3 ful

FULL SEARCH INITIATED 12:56:01 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 352 TO ITERATE

100.0% PROCESSED 352 ITERATIONS

38 ANSWERS

SEARCH TIME: 00.00.01

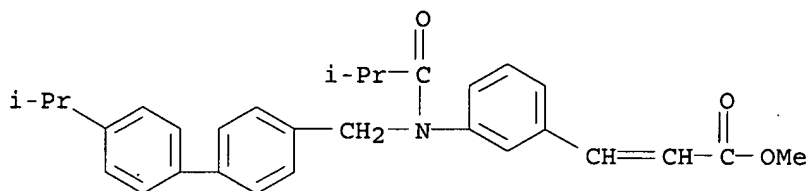
L5 38 SEA SSS FUL L2 OR L3

=> d tot reg

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3	RN	698356-52-4	REGISTRY
4	RN	698356-45-5	REGISTRY
5	RN	698356-39-7	REGISTRY
6	RN	698356-35-3	REGISTRY
7	RN	592526-13-1	REGISTRY
8	RN	592526-10-8	REGISTRY
9	RN	592526-08-4	REGISTRY
10	RN	592526-05-1	REGISTRY
11	RN	592526-02-8	REGISTRY
12	RN	592525-99-0	REGISTRY
13	RN	592525-96-7	REGISTRY
14	RN	592525-94-5	REGISTRY
15	RN	592525-91-2	REGISTRY
16	RN	592525-88-7	REGISTRY
17	RN	592525-85-4	REGISTRY
18	RN	592525-82-1	REGISTRY
19	RN	592525-79-6	REGISTRY
20	RN	592525-76-3	REGISTRY
21	RN	592525-74-1	REGISTRY
22	RN	592525-70-7	REGISTRY
23	RN	592525-68-3	REGISTRY
24	RN	592525-65-0	REGISTRY
25	RN	592525-62-7	REGISTRY
26	RN	592525-59-2	REGISTRY
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33	RN	592525-39-8	REGISTRY
34	RN	592525-36-5	REGISTRY
35	RN	592525-33-2	REGISTRY
36	RN	592525-30-9	REGISTRY
37	RN	574005-64-4	REGISTRY
38	RN	574005-63-3	REGISTRY

=> d 37 36 1 2 3 sub bib abs

LS ANSWER 37 OF 38 REGISTRY COPYRIGHT 2005 ACS on STN
RN 574005-64-4 REGISTRY
ED Entered STN: 27 Aug 2003
CN 2-Propenoic acid, 3-[3-[[[4'-(1-methylethyl)[1,1'-biphenyl]-4-yl]methyl](2-methyl-1-oxopropyl)aminophenyl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C30 H33 N O3
SR CA
LC STN Files: CA, CAPLUS



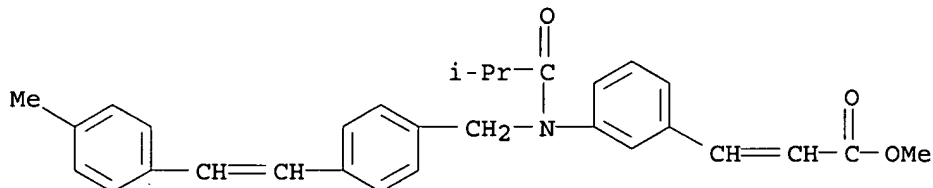
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 139:159454 CA
TI A chemical, genetic, and structural analysis of the nuclear bile acid receptor FXR
AU Downes, Michael; Verdecia, Mark A.; Roecker, A. J.; Hughes, Robert; Hogenesch, John B.; Kast-Woelbern, Heidi R.; Bowman, Marianne E.; Ferrer, Jean-Luc; Anisfeld, Andrew M.; Edwards, Peter A.; Rosenfeld, John M.; Alvarez, Jacqueline G. A.; Noel, Joseph P.; Nicolaou, K. C.; Evans, Ronald M.
CS Gene Expression Laboratory, Howard Hughes Medical Institute, La Jolla, CA, 92037, USA
SO Molecular Cell (2003), 11(4), 1079-1092
CODEN: MOCEFL; ISSN: 1097-2765
PB Cell Press
DT Journal
LA English
AB The farnesoid X receptor (FXR) functions as a bile acid (BA) sensor coordinating cholesterol metabolism, lipid homeostasis, and absorption of dietary fats and vitamins. However, BAs are poor reagents for characterizing FXR functions due to multiple receptor independent properties. Accordingly, using combinatorial chemical we evolved a small mol. agonist termed fexaramine with 100-fold increased affinity relative to natural compds. Gene-profiling expts. conducted in hepatocytes with FXR-specific fexaramine vs. the primary BA chenodeoxycholic acid (CDCA) produced remarkably distinct genomic targets. Highly diffracting cocrystals (1.78 Å) of fexaramine bound to the ligand binding domain of FXR revealed the agonist sequestered in a 726 Å³ hydrophobic cavity and suggest a mechanistic basis for the initial step in the BA signaling pathway. The discovery of fexaramine will allow us to unravel the FXR genetic network from the BA network and selectively manipulate components of the cholesterol pathway that may be useful in treating cholesterol-related human diseases.
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 36 OF 38 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 592525-30-9 REGISTRY
 ED Entered STN: 25 Sep 2003
 CN 2-Propenoic acid, 3-[3-[(2-methyl-1-oxopropyl)[4-[2-(4-methylphenyl)ethenyl]phenyl]methyl]aminophenyl]-, methyl ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C30 H31 N O3
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL



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4 REFERENCES IN FILE CA (1907 TO DATE)
 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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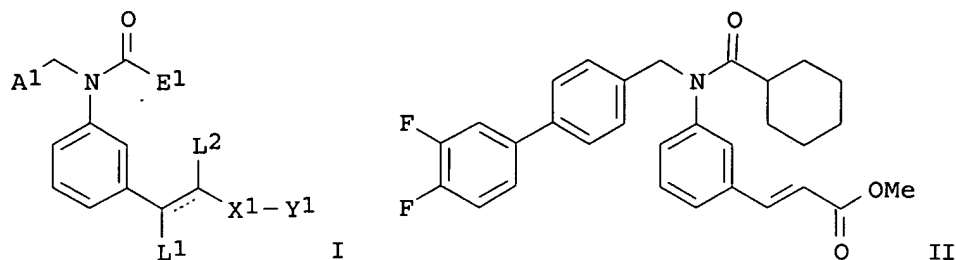
AN 141:23422 CA
 TI Preparation of non-steroidal FXR agonists
 IN Nicolaou, Kyriacos C.; Roecker, Anthony J.; Hughes, Robert; Pfefferkorn, Jeffrey A.
 PA The Scripps Research Institute, USA
 SO PCT Int. Appl., 75 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004046162	A2	20040603	WO 2003-US36195	20031114
	WO 2004046162	A3	20040812		
	WO 2004046162	C1	20050324		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2002-426456P		20021114		
	US 2003-491185P		20030729		

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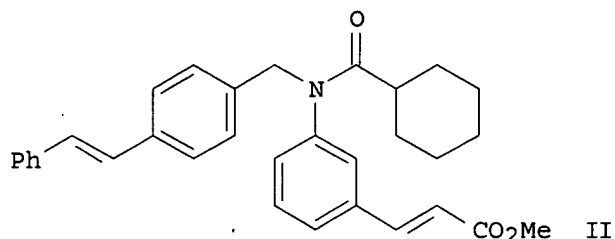
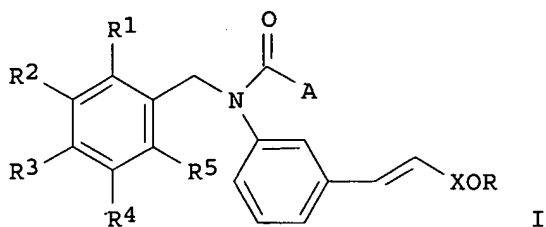
AB Non-steroidal N-aryl-N-arylmethyl amido and ureido compds. such as I [E1 = (C1-C8)alkyl, cyclohexyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, Ph, NH(C1-C8)alkyl; L1, L2 = H; dashed bond = single bond or double bond; X1 = CO, CH2; Y1 = H, NHZ1, NH(Z2)Z3, OZ4; A1 = aryl, heterocyclyl etc.; Z1 = H, Ph, alkyl, benzyl, benzoyl; Z2, Z3 = alkyl; Z2Z3 = cycloalkyl; Z4 = H, oxygen protecting group], were prepared for their therapeutic use as farnesoid X receptor (FXR) agonists. Thus, biaryl compound II, prepared via solid phase synthesis starting from N-(tert-butoxycarbonyl)-3-aminocinnamic acid, Merrifield Resin, 4-bromobenzaldehyde, cyclohexanoyl chloride, and 3,4-difluorobenzeneboronic acid, showed FXR activity (EC50 = 72 nM) and relative efficacy = 1.70 at 1-100 mM CDCA from a cell-based assay. The FXR agonists are useful as therapeutic agents for the treatment of diseases linked to cholesterol, bile acids, and their metabolism and homeostasis.

REFERENCE 2

AN 141:17647 CA
 TI N-acyl-N-arylmethylaniline acrylates as nonsteroidal farnesoid X receptor modulators
 IN Downes, Michael R.; Evans, Ronald M.
 PA The Salk Institute for Biological Studies, USA
 SO PCT Int. Appl., 98 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004046068	A2	20040603	WO 2003-US36137	20031114
	WO 2004046068	A3	20041229		
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	RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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PRAI	US 2002-426664P		20021115		
	US 2003-658115		20030908		

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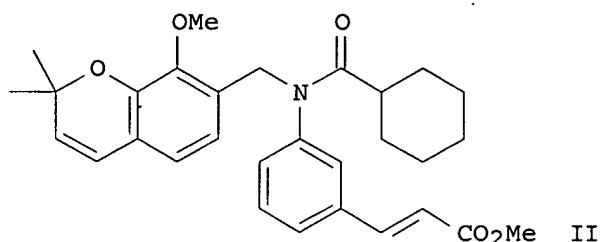
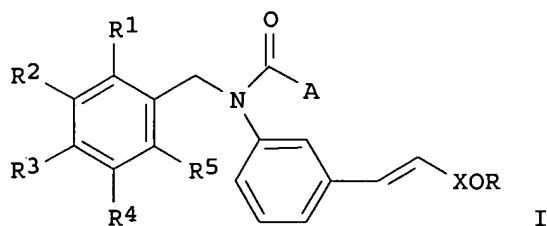
AB A method for modulating process(es) mediated by farnesyl X receptor polypeptides comprises conducting said process(es) in the presence of title compds. [I; A = (substituted) alkyl, cycloalkyl, aryl, heteroaryl; X = CO, CH₂; R = Me, Et; R₁ = H, OH, alkoxy, PhCO₂, mesityloxy, OCH₂CO₂Et; R₂ = H; R₃ = alkenyl, (substituted) aryl, heteroaryl, aralkenyl, heteroaralkenyl; R₂R₃ = atoms to form a (substituted) (unsatd.) pyran ring; R₄ = H, OH; R₅ = H, OH, alkoxy, aryloxy]. In a cell-based transcription assay, title compound (II) activated FXR with EC₅₀ = 36 nM.

REFERENCE 3

AN 141:17646 CA
 TI N-acyl-N-benzylaniline acrylates as nonsteroidal farnesoid X receptor (FXR) modulators
 IN Downes, Michael R.; Evans, Ronald Mark; Hughes, Robert; Nicolaou, Kyriacos C.; Roecker, Anthony J.
 PA The Salk Institute for Biological Studies, USA; The Scripps Research Institute
 SO PCT Int. Appl., 62 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004045511	A2	20040603	WO 2003-US36123	20031114
	WO 2004045511	A3	20040708		
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	RW:				
	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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PRAI	US 2002-426664P		20021115		
	US 2003-658115		20030908		

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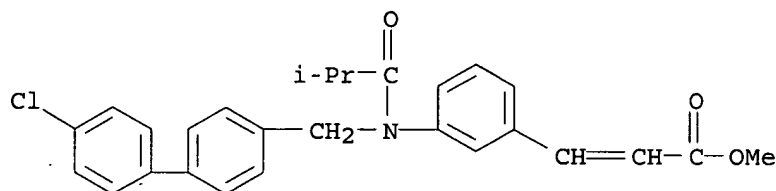
AB Title compds. [I; A = (substituted) alkyl, cycloalkyl, aryl, heteroaryl; X = CO, CH₂; R = Me, Et; R₁ = H, OH, alkoxy, PhCO₂, mesityloxy, OCH₂CO₂Et; R₂ = H; R₃ = alkenyl, (substituted) aryl, heteroaryl, aralkenyl, heteroaralkenyl; R₂R₃ = atoms to form a substituted (unsatd.) pyran ring; R₄ = H, OH; R₅ = H, OH, alkoxy, aryloxy], are claimed. Thus, benzopyran derivative (II) activated FXR receptors with EC₅₀ = 358 nM.

REFERENCE 4

AN 139:224366 CA
 TI Discovery and optimization of non-steroidal FXR agonists from natural product-like libraries
 AU Nicolaou, K. C.; Evans, Ronald M.; Roecker, A. J.; Hughes, Robert; Downes, Michael; Pfefferkorn, Jeffery A.
 CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
 SO Organic & Biomolecular Chemistry (2003), 1(6), 908-920
 CODEN: OBCRAK; ISSN: 1477-0520
 PB Royal Society of Chemistry
 DT Journal
 LA English
 AB The efficient regulation of cholesterol biosynthesis, metabolism, acquisition, and transport is an essential component of lipid homeostasis. The farnesoid X receptor (FXR) is a transcriptional sensor for bile acids, the primary product of cholesterol metabolism. Accordingly, the development of potent, selective, small mol. agonists, partial agonists, and antagonists of FXR would be an important step in further deconvoluting FXR physiol. Herein, we describe the development of four novel classes of potent FXR activators originating from natural product-like libraries. Initial screening of a 10000-membered, diversity-orientated library of benzopyran containing small mols. for FXR activation utilizing a cell-based reporter assay led to the identification of several lead compds. possessing low micromolar activity (EC₅₀'s = 5-10 μM). These compds. were systematically optimized employing parallel solution-phase synthesis and solid-phase synthesis to provide four classes of compds. that potently activate FXR. Two series of compds., bearing stilbene or biaryl moieties, contain members that are the most potent FXR agonists reported to date in cell-based assays. These compds. may find future utility as chemical tools in studies aimed at further defining the physiol. role of FXR and discovering potential therapeutic agents for the treatment of diseases linked to cholesterol and bile acid metabolism and homeostasis.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 1 OF 38 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 858360-31-3 REGISTRY
 ED Entered STN: 04 Aug 2005
 CN 2-Propenoic acid, 3-[3-[[[4'-chloro[1,1'-biphenyl]-4-yl)methyl](2-methyl-1-oxopropyl)aminol]phenyl]-, methyl ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C27 H26 Cl N O3
 SR CA
 LC STN Files: CA, CAPLUS



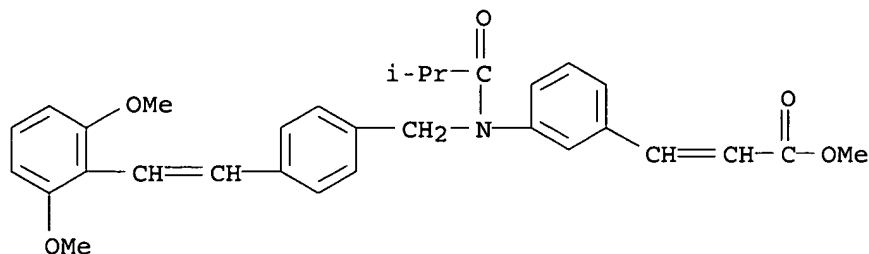
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 143:125843 CA
 TI Hologram quantitative structure-activity relationships for a series of farnesoid X receptor activators
 AU Honorio, Kathia M.; Garratt, Richard C.; Andricopulo, Adriano D.
 CS Instituto de Fisica de Sao Carlos, Centro de Biotecnologia Molecular Estrutural, Laboratorio de Quimica Medicinal e Computacional, Universidade de Sao Paulo, Sao Carlos-SP, 13560-970, Brazil
 SO Bioorganic & Medicinal Chemistry Letters (2005), 15(12), 3119-3125
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier B.V.
 DT Journal
 LA English
 AB The farnesoid X receptor (FXR) is an attractive drug target for the development of novel therapeutic agents for the treatment of dyslipidemia and cholestasis. Hologram quant. structure-activity relationship (HQSAR) studies were conducted on a series of potent FXR activators originated from natural product-like libraries. A training set containing 82 compds. served to establish the models. The best HQSAR model was generated using atoms, bonds, connections, chirality, and donor and acceptor as fragment distinction and fragment size default (4-7) with six components. The model was used to predict the potency of 20 test set compds. that were not included in the training set, and the predicted values were in good agreement with the exptl. results. The final HQSAR model and the information obtained from HQSAR 2D contribution maps should be useful for the design of novel FXR ligands having improved potency.
 RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 38 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 699019-78-8 REGISTRY
 ED Entered STN: 25 Jun 2004
 CN 2-Propenoic acid, 3-[3-[[[4-[2-(2,6-dimethoxyphenyl)ethenyl]phenyl]methyl](2-methyl-1-oxopropyl)aminol]phenyl]-, methyl ester (9CI) (CA INDEX NAME)
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 MF C31 H33 N O5
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

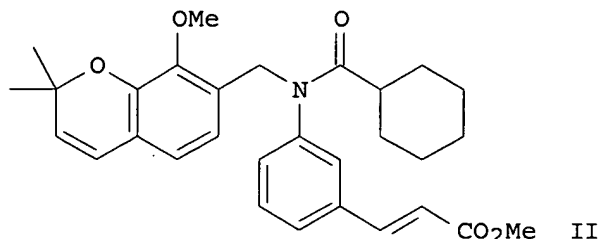
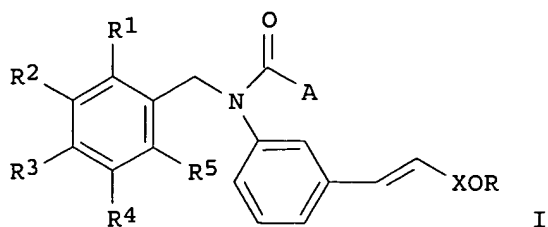
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 141:17646 CA
TI N-acyl-N-benzylaniline acrylates as nonsteroidal farnesoid X receptor (FXR) modulators
IN Downes, Michael R.; Evans, Ronald Mark; Hughes, Robert; Nicolaou, Kyriacos C.; Roecker, Anthony J.
PA The Salk Institute for Biological Studies, USA; The Scripps Research Institute
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004045511	A2	20040603	WO 2003-US36123	20031114
	WO 2004045511	A3	20040708		
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	US 2005143449	A1	20050630	US 2003-658115	20030908
PRAI	US 2002-426664P		20021115		
	US 2003-658115		20030908		

GI



AB Title compds. [I; A = (substituted) alkyl, cycloalkyl, aryl, heteroaryl; X = CO, CH₂; R = Me, Et; R₁ = H, OH, alkoxy, PhCO₂, mesityloxy, OCH₂CO₂Et; R₂ = H; R₃ = alkenyl, (substituted) aryl, heteroaryl, aralkenyl, heteroaralkenyl; R₂R₃ = atoms to form a substituted (unsatd.) pyran ring; R₄ = H, OH; R₅ = H, OH, alkoxy, aryloxy], are claimed. Thus, benzopyran derivative (II) activated FXR receptors with EC₅₀ = 358 nM.

L5 ANSWER 3 OF 38 REGISTRY COPYRIGHT 2005 ACS on STN

RN 698356-52-4 REGISTRY

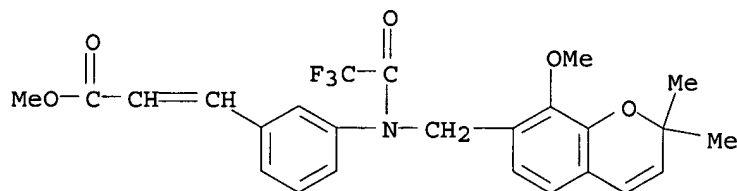
ED Entered STN: 24 Jun 2004

CN 2-Propenoic acid, 3-[3-[[[(8-methoxy-2,2-dimethyl-2H-1-benzopyran-7-yl)methyl](trifluoroacetyl)amino]phenyl]-, methyl ester (9CI) (CA INDEX NAME)

MF C₂₅ H₂₄ F₃ N O₅

SR CA

LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 141:23422 CA

TI Preparation of non-steroidal FXR agonists

IN Nicolaou, Kyriacos C.; Roecker, Anthony J.; Hughes, Robert; Pfefferkorn, Jeffrey A.

PA The Scripps Research Institute, USA

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

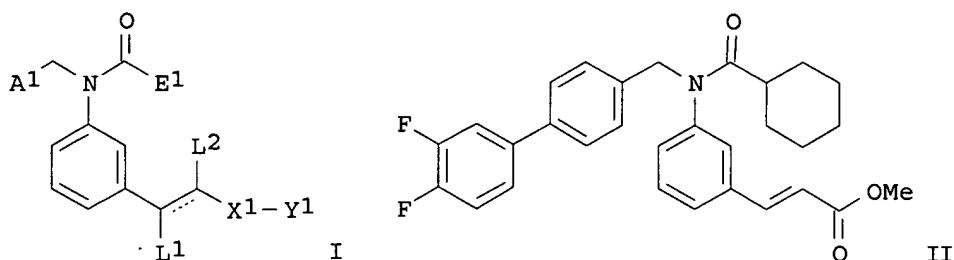
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004046162	A2	20040603	WO 2003-US36195	20031114
	WO 2004046162	A3	20040812		
	WO 2004046162	C1	20050324		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2002-426456P		20021114		
	US 2003-491185P		20030729		

GI



AB Non-steroidal N-aryl-N-arylmethyl amido and ureido compds. such as I [E1 = (C1-C8)alkyl, cyclohexyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, Ph, NH(C1-C8)alkyl; L1, L2 = H; dashed bond = single bond or double bond; X1 = CO, CH2; Y1 = H, NHZ1, NH(Z2)Z3, OZ4; A1 = aryl, heterocyclyl etc.; Z1 = H, Ph, alkyl, benzyl, benzoyl; Z2, Z3 = alkyl; Z2Z3 = cycloalkyl; Z4 = H, oxygen protecting group], were prepared for their therapeutic use as farnesoid X receptor (FXR) agonists. Thus, biaryl compound II, prepared via solid phase synthesis starting from N-(tert-butoxycarbonyl)-3-aminocinnamic acid, Merrifield Resin, 4-bromobenzaldehyde, cyclohexanoyl chloride, and 3,4-difluorobenzeneboronic acid, showed FXR activity (EC50 = 72 nM) and relative efficacy = 1.70 at 1-100 mM CDCA from a cell-based assay. The FXR agonists are useful as therapeutic agents for the treatment of diseases linked to cholesterol, bile acids, and their metabolism and homeostasis.

REFERENCE 2

AN 141:17647 CA
 TI N-acyl-N-arylmethylaniline acrylates as nonsteroidal farnesoid X receptor modulators
 IN Downes, Michael R.; Evans, Ronald M.
 PA The Salk Institute for Biological Studies, USA
 SO PCT Int. Appl., 98 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004046068	A2	20040603	WO 2003-US36137	20031114
	WO 2004046068	A3	20041229		

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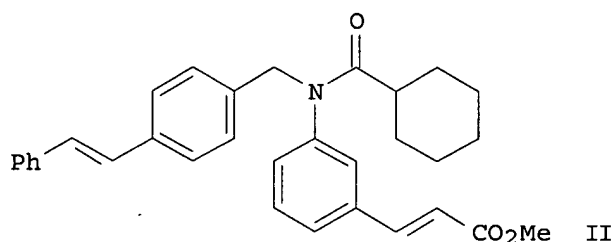
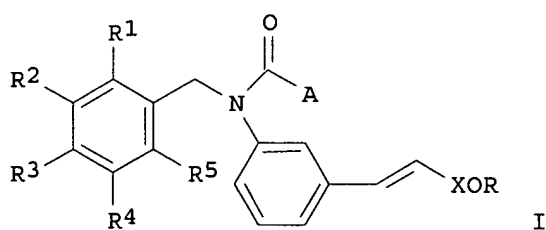
US 2005143449 A1 20050630

US 2003-658115 20030908

PRAI US 2002-426664P 20021115

US 2003-658115 20030908

GI



AB A method for modulating process(es) mediated by farnesyl X receptor polypeptides comprises conducting said process(es) in the presence of title compds. [I; A = (substituted) alkyl, cycloalkyl, aryl, heteroaryl; X = CO, CH₂; R = Me, Et; R₁ = H, OH, alkoxy, PhCO₂, mesityloxy, OCH₂CO₂Et; R₂ = H; R₃ = alkenyl, (substituted) aryl, heteroaryl, aralkenyl, heteroaralkenyl; R₂R₃ = atoms to form a (substituted) (unsatd.) pyran ring; R₄ = H, OH; R₅ = H, OH, alkoxy, aryloxy]. In a cell-based transcription assay, title compound (II) activated FXR with EC₅₀ = 36 nM.

REFERENCE 3

AN 141:17646 CA
 TI N-acyl-N-benzylaniline acrylates as nonsteroidal farnesoid X receptor (FXR) modulators
 IN Downes, Michael R.; Evans, Ronald Mark; Hughes, Robert; Nicolaou, Kyriacos C.; Roecker, Anthony J.
 PA The Salk Institute for Biological Studies, USA; The Scripps Research Institute
 SO PCT Int. Appl., 62 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004045511	A2	20040603	WO 2003-US36123	20031114

WO 2004045511 A3 20040708

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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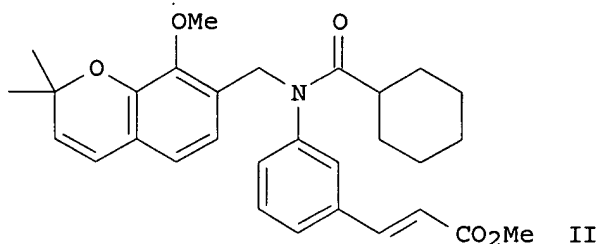
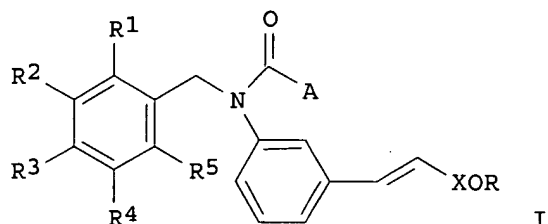
US 2005143449 A1 20050630

US 2003-658115 20030908

PRAI US 2002-426664P 20021115

US 2003-658115 20030908

GI



AB Title compds. [I; A = (substituted) alkyl, cycloalkyl, aryl, heteroaryl; X = CO, CH2; R = Me, Et; R1 = H, OH, alkoxy, PhCO2, mesityloxy, OCH2CO2Et; R2 = H; R3 = alkenyl, (substituted) aryl, heteroaryl, aralkenyl, heteroaralkenyl; R2R3 = atoms to form a substituted (unsatd.) pyran ring; R4 = H, OH; R5 = H, OH, alkoxy, aryloxy], are claimed. Thus, benzopyran derivative (II) activated FXR receptors with EC50 = 358 nM.

=> log h

COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
289.04	289.25

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
-3.40	-3.40

CA SUBSCRIBER PRICE

SESSION WILL BE HELD FOR 60 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 13:01:59 ON 18 OCT 2005